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THE WALTER AND ELIZA HALL INSTITUTE OF RESEARCH IN PATHOLOGY AND MEDICINE

NINTH ANNUAL REPORT

1927-28

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STAFF.

Charles H. Kellaway, M.C., M.D., M.S. (MELB.), M.R.C.P. (LOND.) (Director).

N. Hamilton Fairley, O.B.E., M.D., D.Sc. (MELB.), D.T.M. & H. (CANTAB.), F.R.C.P. (LOND.).

F. M. Burnet, M.D. (MELB.), Ph.D. (LOND.). (Assistant Director).

H. F. Holden, M.A. (CANTAB.). (Research Bio-Chemist).

Miss F. Eleanor Williams.

Miss Mavis Freeman, B.Sc. (MELB.). (Bio-Chemical Research Student).

Miss Lesley Rudd, B.A. (MELB.). (Director's Secretary and Librarian).

Part-Time Workers:

C. J. O. Brown, M.D., B.S. (MELB.), F.R.C.S. (ENG.), Honorary Out-Patient Surgeon to the Austin Hospital.

J. F. Chambers, M.D., B.S. (MELB.), M.R.C.P. (LOND.), Honorary Physician to the Austin Hospital.

H. R. Dew, M.B., B.S. (MELB.), F.R.C.S. (ENG.), F.A.C.S., Honorary Out-Patient Surgeon to the Melbourne Hospital.

K. D. Fairley, M.D. (MELB.), M.R.C.P. (ENG.), Honorary Physician to Out-Patients at the Melbourne Hospital, Clinical Research Scholar.

J. Monahan Lewis, D.D.Sc. (MELB.).

C. H. Searby, M.D., M.S., B.Sc. (MELB.), F.R.C.S. (ENG.), Honorary Out-Patient Surgeon to the Melbourne Hospital, Demonstrator in Anatomy in the University of Melbourne (Cancer Research).

Members of the Staff appointed by the Hospital:

PROFESSOR PETER MACCALLUM, M.C., M.A., M.SC., M.B., Ch.B., D.Ph., Honorary Pathologist to the Melbourne Hospital

C. H. MOLLISON. M.B., B.S. (MELB.), M.R.C.S. (ENG.), Honorary Assistant Pathologist to the Melbourne Hospital.

R. J. WRIGHT-SMITH, M.D., B.S. (MELB.), Senior Resident Pathologist.

MISS LUCY M. BRYCE, M.B., B.S., B.SC. (MELB.), Bacteriology.

MISS BERYL SPLATT, B.SC. (MELB.), Bio-Chemistry.

MISS CECIL MAUDSLEY, B.SC. (MELB.), Electro-Cardiography, Basal Metabolism.

E. G. DAHLENBURG, M.B., B.S. (MELB.), Pathological Registrar

We have sustained a grievous loss by the recent death of our Chairman, Sir Aaron Danks. Among the many public matters which continuously engaged his attention, the affairs of this Institute held a prominent place. He found time to get to know personally all the members of the Staff, and was always ready with advice and practical help in any problem that faced us. Much of the progress which the Institute has made in the last few years has been due to his never-failing interest and encouragement. The Institute has lost a stalwart supporter and we a tried and trusted friend.

The Ninth Annual Report

OF THE

Walter and Eliza Hall Institute of Research

July, 1928.

This year has been an important one in the history of the Institute. For the first time its value has been recognised by the Commonwealth Government—firstly, by the allotment of a grant of £2,500 for researches carried on here on behalf of the Commonwealth Department of Health; and, secondly, by the appointment of the Director of the Institute as Chairman of the Royal Commission of Inquiry into the fatalities at Bundaberg.

But for the generosity of the Edward Wilson ("The Argus") Trust it would not have been possible to carry on the work of the Bio-Chemical Department, since the endowment fund instituted by the late Sir Aaron Danks, owing to various causes, has made but little progress this year. Their gift of £1,500 repeated this year has enabled us to continue and develop this important part of our activities. The Felton Trust has also again come to our assistance by a contribution to our general fund.

The future of the Institute will naturally depend upon the money available for its development, and it is an encouraging sign that during the last three or four years public-spirited citizens have recognised the value to the community of medical research by making bequests which will ultimately be applied to the work in this Institute.

We are fortunate in still having with us Dr. N. Hamilton Fairley, who has undertaken the direction of several of the researches which are being carried out for the Commonwealth Government, on bilharzia, on hydatid disease, on the venomous snakes of Australia, and on the incidence of certain diseases in the domestic herbivora. Dr. Fairley has recently received the Doctorate of Science of the Melbourne University, has been elected a Fellow of the Royal College of Physicians (London), and has been appointed a member of the staff of the Tropical Diseases Hospital, London. He will be leaving us at the end of the year, and, it is hoped, will represent the Institute at the International Congress of Tropical Medicine and Hygiene at Cairo.

In January, Dr. F. M. Burnet, who has been appointed Assistant Director, returned from England, where he had been working at the Lister Institute. He had, just before sailing, obtained the Ph.D. of the London University for his researches carried out there on "Smooth and Rough Variations in Bacteria in Relation to Bacteriophage." He is taking charge of the bacteriological side of the work of the Institute.

Mr. Holden, who is in charge of the bio-chemical department, has obtained the services of Miss M. Freeman, B.Sc., as Bio-Chemical Research Fellow at this Institute.

Dr. T. Cherry, the John Grice Cancer Research Fellow, who for the last three years has been working here on the effect of the injection of minute doses of tubercle bacilli into mice and has obtained some interesting results reported elsewhere, left us at the end of February to continue his researches on a more extensive scale at the Veterinary Institute.

Dr. Lucy Bryce, who has been working here for the last eighteen months for the Obstetrical Research Committee, is now taking charge of the routine bacteriology for the Hospital.

Miss Marjorie Shannon has been helping Miss Splatt in routine bio-chemical work in an honorary capacity. Miss Francis Eales left us at the end of the year, and Miss Lesley Rudd was appointed in her place as Librarian and Secretary to the Director. Miss Flockhart has left us to take an appointment at the Geelong Hospital.

The Work of the Institute.

Experimental Work Connected with the Bundaberg Inquiry.

The Royal Commission of Inquiry into the fatalities at Bundaberg, appointed on February 1st, 1928, consisted of the Director of this Institute (Chairman), Professor P. MacCallum, Professor of Pathology in the Melbourne University; and of Dr. A. H. Tebbutt, Pathologist of the Royal Prince Alfred Hospital, Sydney. Most of the experimental work in connection with this inquiry was carried out at this Institute.

On January 27th, at Bundaberg, Queensland, eight children from 1¼ to 7½ years of age received subcutaneously 4 minums of diphtheria toxin-antitoxin mixture, of whom six died, two were ill but recovered, and subsequenty developed local abscesses at the site of inoculation. Thirteen children from 2½ to 9½ years of age received 2 minums, of whom six died, four were ill and afterwards developed abscesses, and three not ill but subsequently developed abscesses at the site of inoculation. The symptoms presented in nearly all the cases appeared from five to eight hours after the injection, though in two which recovered the time of onset was fifteen and twenty hours respectively. There was early vomiting and diarrhoea, followed later by unconsciousness, shallow rapid breathing, cyanosis, and pyrexia. In the younger children there were convulsions, and in the older ones twitching and restlessness. In many there was late vomiting of a cerebral type. In two there was a generalised skin rash. There seems to have been no general rigidity between the convulsions, and the symptoms were not those of tetanus. The deaths, with one exception (34 hours), occurred between fifteen and twenty-five hours after inoculation. There were no paralyses, no squints, and no evidence of meningeal involvement. In the cases which recovered, local reaction at the site of inoculation was early evident. There was, however, nothing suggestive of an infiltration due to excess of diphtheria toxin.

The post-mortem findings were, unfortunately, incomplete, though autopsies were carried out at Bundaberg in nine cases and some material was kept. There were no gross macroscopic lesions apart from ante-mortem thrombi in the large veins in one or two cases. Professor P. MacCallum, at the Institute, made a careful study of the material available, and found that the most striking features were degenerative changes in the lymphatic follicles of glands, intestinal mucosa and Malpigian bodies of the spleen, and phagocytosis by proliferated endothelial cells.

In some lymph glands which were much engorged there was dilation of the afferent lymph sinuses which contained many polymorph leucocytes. There was some cloudy swelling of the liver and kidneys, some congestion, and, in some of the portal tracts, excess of leucocytes. The suprarenals and thymus were normal.

The children came from widely separated homes and had been congregated at no place at any recent time other than that at which the injections were made. They were not all present at the same time during the period of about an hour in which the injections were made. They had partaken of no common food or drink. Dr. F. M. Burnet found that the sera of the survivors did not agglutinate organisms of the Salmonella group.

Examination of the organs from two of the fatal cases by Mr. H. F. Holden demonstrated the absence of heavy metals in significant amounts.

The sample of toxin-antitoxin mixture from which the injections had been made contained no antiseptic. It was enclosed in a rubber-capped bottle, and had been used on four previous occasions for the inoculation of children at Bundaberg without any ill effects resulting. The remainder of the mixture submitted to us for examination contained no obvious excess of diphtheria toxin. No anaerobes could be isolated from it, though carefully tested media and rigid technique were used. Except for a few yeasts which were seen in smears, but which we were unable to cultivate, it contained only a staphylococcus, which was later found by Dr. F. M. Burnet to be identical with Hine's type II., No. 1393, of the national collection of type cultures at the Lister Institute. This organism was present in considerable numbers. It was found to be only of average virulence for mice and guinea pigs and monkeys (macacus rhesus). It was, however, variably pathogenic for rabbits, and, immediately after its inoculation and growth in toxin-antitoxin mixture of a similar batch, killed in relativley small doses with convulsions and without lesions, even in so short a time as eleven hours.

This staphylococcus was proved by Dr. F. M. Burnet to be identical with that isolated in a pure culture from the abscesses in all those children which were examined. The identity of these staphylococci was shown by their agglutination reactions with sera made from cultures of the organism isolated from the Bundaberg bottle, by the exhibition by all the cultures of the Müller phenomenon (the appearance of a zone of punctuate haemolysis round the colonies on hormone blood agar), and by their specific reactions to a bacteriophage active against the strain from the Bundaberg bottle.

Experiments were also carried out by Dr. Burnet on the production of a skin-reacting toxin by the Bundaberg staphylococcus. When the organism was grown even for short periods (seven to eight hours) in broth to which human blood had been added, the filtrates from the cultures in dilutions of 1 in 500 to 1 in 2,000 gave good skin reactions in susceptible individuals. About half the individuals tested were found to be sensitive. Comparison with filtrates prepared from other pathogenic staphylococci indicated that these reactions were specific, and later unpublished experiments have demonstrated that the sera of some insensitive individuals can protect against the toxin. These skin-reacting filtrates were found to have no toxic effects when injected into laboratory animals.

Dr. Tebbutt made some careful studies of the rate of growth of the Bundaberg organism in toxin-antitoxin mixture at Bundaberg temperatures, and at the same time observed the result of the subcutaneous injection of the mixture at various periods into guinea pigs and monkeys. In guinea pigs injected with the mixture, after five or six days' incubation, an extensive cellulitis was produced. This phenomenon could not be related to the number of living organisms injected. Increasing doses of emulsions of the staphylococcus grown on agar mixed with sterile toxin-antitoxin mixture or broth, and immediately injected, produced similar effects, if the doses of organisms were large enough. The phenomenon was therefore thought to depend on the number of living and dead organisms present. Similar increase in activity of the infected mixture was also shown in experiments on monkeys. These studies were of particular interest in view of the fact that the infected mixture appeared to reach maximal activity at about the fifth or sixth day.

We were further concerned with the question as to whether it were possible that other more delicate pathogenic organisms might have been present in the mixture, which, in the presence of the hardier staphylococcus, failed to grow when the remaining mixture was cultured by us a week after the tragedy. We found that the organisms we used in these experiments readily survived when grown with the staphylococcus in toxin-antitoxin mixture, and could be recovered by culture after ten days. More especially was this so in the case of B. tetani. No appreciable amount of tetanus toxin was produced under these conditions.

Among the most laborious of our investigations were those directed towards determining whether diphtheria toxin played any part in causing the deaths at Bundaberg. The sera of the children who recovered were carefully titrated to determine their content of antitoxin, since we were obviously unable to Schick test the children themselves. This was done by intradermal and protection tests on guinea pigs, and the sera of a group of Schick tested children of like ages were investigated similarly as a control.

The Bundaberg survivors were divisible into three groups: (1) Two children who had no symptoms—one had a high and one a low titre of antitoxin; (2) those who had symptoms and recovered, but had had antitoxin administered in hospital; these—three in number—had a moderately high titre of antitoxin; (3) those who had severe symptoms but received no antitoxin; these had a very low titre, and would have been Shick positive if tested.

Further studies were directed to the investigation of the possibility of the dissociation of toxin-antitoxin by the growth of organisms in it. A number of different organisms were used for this purpose, notably B. proteus x 19, on account of its known proteclytic activities. We were unable to demonstrate any trace of dissociation with any of the organisms used. Experiments with the Bundaberg staphylococcus were invariably negative.

The growth of the Bundaberg organism was also studied in toxin and antitoxin separately. These were made up in approximately the same concentrations and at the same pH as in toxin-antitoxin mixture. The content of these solutions in toxin and antitoxin was separately estimated by the use of intradermal and protection methods of titration. No appreciable destruction was caused in toxin by the growth of the staphylococcus in nineteen days at Bundaberg temperatures, and the deterioration of antitoxin under these conditions, though evident, was not very striking.

Experiments were also made to determine whether free diphtheria toxin in sublethal doses, injected together with emulsions of living staphylococci, could cause death in experimental animals when the same dose of staphylococci alone failed to do so. This was found not to be the case. No evidence was obtained in any of our experiments to show that diphtheria toxin played any part in causing the deaths at Bundaberg.

Experiments were also performed on air contamination. It was shown that in still air with rigid technique it was possible to inject air in moderately large quantities into bottles of toxin-antitoxin mixture in which antiseptic was present, without contamination occurring. When the air in the room was set in motion by means of an electric fan, air contamination occurred in a high percentage of cases. The presence of 0.5% phenol was found to inhibit the growth of organisms introduced in this way, and it was shown that the Bundaberg staphylococcus would not grow in toxin-antitoxin mixture in which phenol was present in this concentration.

Iodine had been used to sterilise the top of the rubber cap of the Bundaberg bottle, and Mr. H. F. Holden was able to show that the remaining liquid contained an appreciable amount of iodine. This was of interest as indicating the ease with which liquids used for sterilising the rubber cap, and organisms, if these were present on the surface, could easily be passed into the interior of the bottles through their rubber caps when needles were inserted through them.

Bacteriological Studies.

The bacteriological side of the work of the Institute is now in the capable hands of Dr. F. M. Burnet. Since his arrival in January of this year he has mainly been occupied in research on the pathogenic staphylococci, examining the relationships between their antigenic structure, sensitiveness to bacteriophage, and virulence. The work is planned to follow similar lines to that which he has already carried out while working at the Lister Institute on members of the Salmonella group. So far, most of the time has been occupied with work of a preliminary nature—manufacture of sera, acquisition of suitable bacteriophage, and so on. Two other effects of staphylococcal products are under study, both having come under notice in connection with work undertaken for the Bundaberg Commission. These are: (1) the Müller phenomenon, an appearance of discrete areas of haemolysis on human blood agar plates inoculated with staphylococci; and (2) the power of certain strains to produce a substance giving strong skin reactions in sensitive human individuals.

The results of the Bundaberg investigation have brought into prominence the apparently qualitative differences in pathogenicity of staphylococci in human subjects on the one hand and laboratory animals on the other. In these two phenomena we have an action on two forms of human cells or tissues which are not shown with any of the laboratory animals so far tested. It is hoped that investigations along these lines therefore may show some light on the differences in virulence observed.

Preparations have also been made for some studies on anterior poliomyelitis for the Commonwealth Government; a good supply of material is now available, and the virus is being "passaged" through monkeys.

Puerperal Infection.

In 1925 the Obstetrical Research Committee of the Melbourne University was founded, to advise on the expenditure of a gift of £10,000 made by the Edward Wilson ("The Argus") Trust for the purpose of reducing maternal mortality and morbidity in this State. As one part of its activities, the Committee decided to have an investigation made on the bacterial flora of the female genital tract in septic cases and in normal pregnant women, both before and after labour. While it was fully realised that much of this kind of work had already been done in other countries, it was considered that differences due to local hygienic and climatic conditions might be revealed by such an investigation in Australia. In November, 1925, this study was commenced here by Miss F. E. Williams, working in co-operation with Dr. E. R. White of the Women's Hospital, who assumed responsibility for the collection of the material and for the clinical side of the work. Unfortunately, Miss Williams, after about three months, had to abandon the research owing to a serious illness. It was recommenced in August, 1926, by Dr. Lucy Bryce, and completed in April, 1928.

In July, 1927, Dr. White published a paper dealing with treatment and with some clinical aspects of puerperal sepsis, in which some of the results of the bacteriological studies of Miss Williams and Dr. Bryce were utilised. A full account of these researches is now being published. Briefly, the main results are as follows:—

In fifty morbid cases following childbirth or abortion which were examined only post partum, streptococci were the most frequent inhabitants of the uterus, being present in 36%. Five of the six haemolytic strains occurred in pure culture, and four were associated with severe illness. Generally non-haemolytic strains were associated with milder degrees of illness. Gonococci, present in the uterus in 8%, were also associated with fever of a characteristic type. Other organisms found—staphylococci, unidentified Gram-positive and Gram-negative cocci, B. Welchii and other anaerobes and B. Coli could not in the cases studied be related casually to any definite morbid condition.

Cervical cultures were obtained in 119 patients during pregnancy, but in only 103 was the subsequent history available. Various organisms were found. Dr. Bryce has discussed the results from two standpoints: (1) the possibility of infection during labour by organisms already present in the genital passages; and (2) the ability of the normal vaginal secretions to exert a bactericidal action on organisms which might be introduced. In regard to the possibility of endogenous infection, special attention has been focussed on the streptococci which were found in 24 cases, only two of which were febrile in the puerperium, while 79 cases in which they were absent included six febrile cases. Dr. Bryce concludes that it is unsound to relate the presence of streptococci, without consideration of their biological characters or of other factors, to any disease that may be present.

No certainty has been attained as to whether or no the vaginal secretion exerts any bactericidal influence upon individual organisms. The presence of other bacteria of various kinds and in large numbers may be dependent upon their frequent introduction from without, and the occurrence of morbidity may depend on the resistance of the host rather than on any antagonistic properties of the secretion.

Finally, a series of 30 cases previously studied during pregnancy were further examined during the first stage of labour and in the puerperium up to the twelfth day. The flora early in labour does not differ from that found during pregnancy, but it is widely different in the puerperium. The organisms are less numerous in the early days than subsequently. Streptococci, staphylococci, diphtheroids and coliform organisms are present in normal cases. Many of these organisms are saphrophytes which temporarily invade the normal puerperal uterus.

Dr. Bryce, in the course of this work, has had the opportunity of studying various types of the "vaginal bacillus." These organisms were present in about 75% of the 119 cases examined during pregnancy. They were isolated in 64 cases, in 12 of which they were unassociated with other organisms. A more extensive study of ten strains was made. These appear to belong to three groups, corresponding more or less closely to Rahe's types A, B and C of the Lactobacillus acidophilus. Of the 75 cases in which vaginal bacilli were present before the completion of labour, 5% were febrile during the puerperium, and of 28 in which the bacilli were absent, 14% were febrile. These figures, though small, suggest that either the bacillus itself or the vaginal secretion in which it flourishes, may play some part in preventing the growth of introduced pathogenic organisms. On the other hand, the diminished incidence of the bacillus in febrile cases may be significant of changes in the vaginal flora caused by the introduction of pathogenic organisms.

In association with Dr. Marshall Allan, the Director of Obstetrical Research, Dr. Bryce investigated a small outbreak of septic infection occurring in a private nursing home. Between April 23rd and June 30th four cases of infection, three of which were fatal, occurred. One was a fatal puerperal septicaemia, and the others were severe septic infections in newly-born infants. In all cases streptococci were isolated, and in two which were available for examination the organism found presented unusual features, and was identical with a streptococcus isolated from the nasopharynx of a nurse who had an infected antrum.

BRYCE, LUCY M.:

"Some Observations on the Bacterial Flora of the Female Genital Passages in Pregnancy and the Puerperium, with Special Reference to Puerperal Infection."

Medical Journal of Australia (In the Press).

"A Note on the Varieties of Vaginal Bacilli met with in an Investigation on the Flora of the Female Genital Passages."

Medical Journal of Australia, June 30th, 1928.

ALLAN R. MARSHALL and
BRYCE, LUCY M.:

"A Report on an Epidemic of Septic Infection Occurring in a Maternity Hospital."

Medical Journal of Australia, March 3rd, 1928.

The Bio-Chemical Department.

This department of our activities is being directed by Mr. H. F. Holden, and in addition to the more strictly chemical researches being carried out there, a great deal of help has been afforded to workers engaged in various biological problems in other departments. In association with the Director, attempts are being made to recover and estimate extremely small amounts of substances like histamine capable of causing stimulation of plain muscle. This research had unfortunately to be abandoned temporarily owing to the pressure of other work. In association with Dr. N. H. Fairley and Miss Williams, the problem of the association with the globulin fraction of serum, of antibody responsible for complement fixation in hydatid infestation is being investigated. For this purpose Mr. Holden has carried out the necessary protein fractionations of various sera.

The more purely chemical problems studied have been concerned with the constitution of globins derived from the haemoglobins of mammalian blood. In this connection researches have also been commenced on the denatured globins formed from them by simple methods, with a view to gaining some insight into the phenomenon of protein denaturation, which would seem to have aspects in common with such occurrences as the coagulation of blood and the formation of the more important structural proteins of muscular tissue. In this connection our thanks are especially due to Professor W. A. Osborne for the loan of valuable apparatus from the Physiology Department of the Melbourne University, which has been used in these researches.

For the rapid optical estimation of substances whose solutions show well-defined absorption bands in the visible region of the spectrum, Mr. Holden has devised a simple spectro-colorimeter. He has also investigated the applicability of this instrument to the determination of the concentration of oxyhaemoglobin in solutions containing it, and to the determination of the concentration of globin in solutions by titration with haematin.

HOLDEN, H. F.:

"A Simple Spectro-Colorimeter."

Australian Journal of Experimental Biology and Medical Science, 1927, Volume 4, p. 221.

Australian Venomous Snakes.

On returning to Australia last year, Dr. N. Hamilton Fairley, who has had considerable experience with snake bite in India, drew attention to the fact that during the past two decades little work has been done on the Australian venomous snakes, and that despite the general advances made in serum therapy, Tidswell's experimental work on the production of antivenine in this country had not been followed up. The low death rate has no doubt been a factor in this inertia, but many deaths could and would have been prevented had antiserum been available for general use. The fundamental difficulty in the production of antivenine lies in procuring adequate supplies of venom, and with this in view, arrangements were made with the Committee of the Zoological Gardens and the Director, Mr. Wilkie, for the housing of snakes there, and also for the services of Mr. T. E. Eades in collecting and caring for these reptiles. From November to April adequate supplies of tiger snakes and copperheads from Victoria and of death adders from South-western Queensland were procured by Mr. Eades, while a limited number of brown and black snakes were also obtained for the collection. One of the less common species of poisonous snakes, *Pseudechis gutatus*, is also under investigation.

Snake venom has been collected by Dr. Fairley at regular intervals, the poison being immediately dried *in vacuo* over sulphuric acid and subsequently weighed by Miss Splatt.

Sufficient stores of tiger and death adder venom are now available for the first year's immunisation of horses, and arrangements have been made with Dr. F. G. Morgan, Director of the Laboratories Division, Commonwealth Health Department, to start producing antivenines at the Commonwealth serum laboratories for our two most formidable and lethal snakes. This work will be carried out in co-operation with this Institute.

A large number of observations are already available on the venom yields of snakes, shortly after being caught, as well as after weeks or months of captivity. Care has been taken to differentiate between the quantity of poison injected during an actual bite or series of bits and the reserve venom obtained by digital pressure on the venom glands—a procedure technically known as "milking."

The poison yield has been found to vary with different species as well as with individual members of the same species. Tiger snakes give from 5 to 60 mg. of dried venom at the first bite, the maximum total yield obtained after milking being 155 mg. With death adders the yield is generally larger. The quantity injected at the first bite varies from 10 to 130 mg., the total maximum yield equalling 205 mg. The copperhead gives a total yield of from 5 to 85 mg. of dried venom. Fortunately, in captivity both tiger snakes and death adders continue to give satisfactory quantities of poison for many months, but in the case of copperheads and black snakes kept in glass cages away from sunlight, fresh air and running water, the yield has been found to depreciate, and in time disappears altogether. With the brown snake this venom depreciation in captivity is much more rapid and pronounced, and unless open-air accommodation be obtained during the warmer weather, or ultra-violet irradiation, such as that utilised at the London Zoo., be adopted in Melbourne, there is little likelihood of obtaining adequate quantities of venom from this species.

During autopsies on snakes Dr. Fairley found that death was generally caused by lung flukes, and it was also observed that fluke-infested snakes were poor venom producers. Starvation and drought act in similar fashion. In one batch of snakes from the Mitta Valley, where food was plentiful and fluke infestation minimal, high venom yields were met with, whereas in another batch collected in February on the

Murray Downs Station, 11 miles from Swan Hill, shortage of food and water, along with lung fluke disease, had so reduced the venom yield that numbers were practically non-poisonous.

A new approach to the study of ophidian dentition and the mechanism of bite has been opened up by the application by Dr. Fairley of modern dental technique to the reptilia. As a routine procedure with every snake, a series of impressions of the actual bite are taken in dental wax (Kerr's impression compound), and demonstrable records are thus available regarding both the number and position of the fangs, as well as the post maxillary, the palatine and the mandibular teeth. The distance between the fangs is always accurately measured. With the assistance of Dr. A. Mason Cox, D.D.Sc., amalgam models are being constructed so as to demonstrate the actual position of the fangs during penetration of the substance bitten.

In all Australian snakes the fangs are convex, grooved anteriorly and point backwards, and, with the exception of the death adder (which possesses fangs about ¼″ in length, of similar dimensions to the cobra), they are short, often not exceeding ⅛″. Several conclusions of practical importance have resulted from this series of observations. Firstly, the venom yield is found to be definitey correlated with the interval separating the fangs, and it therefore follows that measurements of the fang marks on the skin will have an important prognostic bearing. If the distance does not exceed 1 cm. the amount of poison which has been injected is not likely to be large, but if it is greater than 1.5 cm. several lethal doses are likely to have been deposited in the subcutaneous tissues—at least, so far as the death adder, tiger snake and copperhead are concerned. Then again, the dental impressions show conclusively that though two skin punctures are the rule, sometimes only one, and at other times three puncture marks may be met with, the former depending on an absent or broken fang, the latter on the presence of an advanced reserve fang on one side. Finally, the casts show that though the fangs always point backwards, they are not invariably directed straight backwards. Their course may be directed externally, and under these circumstances a linear incision at right angles to a line joining the punctures would fail to open up the poison pocket. Excision of a limited area encircling the bite is undoubtedly a safer procedure.

We have recently found that 0.23 mg. of tiger snake venom is sufficient to kill a sheep and 3 mg. a horse. This means that in the case of the maximum yield (155 mg.), enough venom was obtained at one milking from a single snake to kill over 600 sheep or 50 horses. Just how many lethal doses this would amount to in man is of course unknown, but it would probably not be much below the figures obtained for the horse. Sir Charles Martin showed that in rabbits immediate ligature was a life-saving device when limited quantities of black or brown snake venom had been injected subcutaneously, and that this procedure was followed by recovery if the amount injected did not exceed six minimal lethal doses. Many tiger snakes must frequently inject much larger quantities of venom than this, and experiments on the effects of ligature in sheep inoculated with varying amounts of the different venoms are being undertaken.

Accurate quantitative studies of the certainly lethal doses for various laboratory animals and an analysis of the toxic effect of these venoms are being undertaken by the Director, and comparison with other venoms is being made. For use in these experiments we are particularly indebted to Col. F. P. Mackie, O.B.E., I.M.S., Director of the Haffkine Institute, Bombay, for a quantity of the venoms of the cobra and of Russell's viper.

Incidentally these observations on a number of different species have already brought to light several new and important facts in regard to the effects of Australian snake venoms. There are variations both in the symptoms produced and in the naked eye pathological findings in different animals using the same venoms, and in the same species of animal using different venoms, which throw light on the complex nature of these poisons, an aspect of the problem which will form the subject of future studies from this Institute.

The observations of earlier workers, notably those of Sir Charles Martin and Dr. Frank Tidswell, have been confirmed and extended. There can be no question that the venom of the tiger snake is more potent in all the species tested than any other known venom with the possible exception of the sea snake *Enhydrina valakadyen*. Those of the death adder and copperhead, while less venomous, are extremely potent. Black-snake venom, on which Professor Sir Charles Martin did much of his early work, is much less poisonous. The venom of *Pseudechis gutatus* already referred to, is intermediate in its toxicity between that of the first three snakes mentioned and the black snake.

An extensive histological investigation of the effects of the Australian snake venoms is being undertaken by Professor Peter MacCallum.

Disease Incidence in the Herbivora.

The absence of accurate data regarding the incidence of certain diseases such as hydatid, liver fluke, tuberculosis and actinomycosis in cattle, sheep and pigs in Australia has constituted a hiatus in both medical and veterinary knowledge which has long required filling, and early in the year it was decided that Dr. Fairley, working in conjunction with Mr. Penrose, B.V.Sc., Medical Superintendent of the City Abattoirs, should undertake such a survey. Extra meat inspectors and clerks were employed to ensure the compilation of accurate records. Over 50,000 sheep have been carefully examined for hydatid, liver fluke, lung worm, cysts of tenuicollis and infective lymphadenitis, and these data are now being analysed with special reference to the age, sex and breed of the particular animals implicated. The surveys of pigs and cattle have been completed, and the analysis shows that out of 4,922 cattle, 45.6% were infected with one or more of the following diseases, the actual rate per thousand being 362.5 for liver fluke, 239.3 for hydatid, 27 for actinomycosis, and 39 for tubercle. The incidence of bovine tubercle increased with age, and in a series of 2,475 cattle from 4½ years upwards the rate equalled 62 per 1,000, or 6.2 **per centum.** Included in this series were numbers of old dairy cows, and the findings have a special significance in connection with the contamination of milk for human consumption by bovine tubercle. Hydatid, liver fluke and actinomycosis showed a similar increase in older animals. Pigs were much freer from all these diseases than cattle, and in a consecutive series of 2,497 animals only 38 were infected, 21 having tubercle, 13 hydatids, 2 liver fluke and 2 actinomycosis.

Hydatid Disease.

Dr. N. Hamilton Fairley and Dr. Wright Smith have made a detailed investigation of the pathology of hydatid in a series of 600 sheep. The cysts totalled 6,497, giving an average distribution of 10.8 cysts per animal. In contradistinction to the findings in man, they were slightly more common in the lungs than the liver, the ratio being 1.3 : 1.0. In 1923 Dr. D. K. Fairley, working at this Institute, found a higher incidence for human cysts in the right than in the left lung, and a similar state of affairs holds in the sheep, the actual ratio being right : left = 1,995 : 1,460 or 1.36 : 1.0.

Of the total cysts examined 13.57% were degenerated, while 86.43% constitute healthy specimens containing brood capsules and scolices. The incidence of degeneration varied in different situations, the actual figures for the liver cysts being 8.68% and for the lung 17.85%. This tendency was equally marked in the two lungs, the right presenting 17.77% and the left 17.94% of the degenerated cysts.

The findings regarding daughter cysts were important, 145 examples being studied. Of these 116 were exogenous and 29 endogenous in origin. Only 27, or 78.6%, occurred in the liver. When daughter cysts of endogenous origin were present, degeneration and collapse of the mother cyst was never observed. Such a finding is explicable only on the basis of absence of overcrowding of endogenous daughters in a short-lived host. The adventitia in these cysts was generally healthy, and evidences of sclerosis and calcification were no more frequent than in cysts of corresponding size in which daughter cysts were absent. These findings in mother cysts containing young endogenous daughter cysts do not support the view that injury and collapse of the mother cyst is a necessary antecedent of daughter cyst formation. Microscopical evidence and histological observations support Dévé's view that the chief, if not the only, source of origin of the endogenous daughter cyst lies in the scolex.

Of the 116 cysts producing exogenous daughters, 22, or 19%, showed degeneration. This aspect of the subject has been especially studied in cattle, in which every phase of their evolution is plainly written. In the earliest stages a few small exogenous cysts are found between the smooth adventitia and the mother cyst. These grow and increase in number. Mechanical separation of the mother cyst from the adventitia occurs locally, and tesselation of the latter begins. Later still a greater area of the mother cyst fails to make contact with the adventitia, the walls of which may be pitted from pressure of exogenous daughters. Finally, the mother cyst degenerates and dies, being found in a central position surrounded by tightly packed daughter cysts encased in a tesselated, pitted or even a pouched adventitia. Here the mechanical separation of the mother cyst from the source of nutriment is the casual factor in its demise.

One other very interesting aspect of the comparative pathology of hydatid was studied first in pig cysts, where clear cystic swellings occurred either singly or in clusters in the laminated layers. Similar forms have since been found in the ectocyst of bovine, ovine and human cysts, and these cyst-like structures can be demonstrated after complete removal of the endogenous layer. At first they were regarded as evidence supporting the intra-cuticular origin of daughter cysts, but detailed study has since shown that they are in reality pseudocysts which never contain hydatid elements or attain a separate existence as independent entities by complete pediculation and separation from the adventitia. They probably originate as a hydropsical or mucoid degeneration of the more central areas of the laminated layers, and in extreme instances lead to a widespread honeycombing of the ectocyst. We suspect that it is this condition, the true nature of which now appears to be recognised for the first time, which has constituted the basis of the old and much supported view regarding intracuticular and endogenous daughter cysts.

Scolex Extracts as Antigens.

A considerable amount of work has been done during the year on the antigenic value of alcoholic and saline extracts of scolices in various immunological reactions in hydatid disease.

The scolex as a source of antigen was first demonstrated in this Institute (in 1921) by Dr. N. Hamilton Fairley, who employed a twenty-four hours' alcoholic extract of wet scolices for complement fixation tests. The necessity for careful standardisation in the presence of syphilitic sera was emphasised. Later Dr. S. W. Patterson and Miss Williams increased the period of extraction to four days, and reported highly satisfactory results in a large series of cases. Production on a commercial scale, using the latter method, was undertaken by the Commonwealth Serum Laboratories, but, unfortunately, after a short trial its manufacture was given up owing to reports that pseudopositive reactions were given by syphilitic and sarcomatous sera. It is well known that alcoholic extracts of any tissue or parasite, if used in sufficient concentration, may act as a Wasserman antigen, and for the past twelve months this problem has received detailed attention at the hands of Dr. Fairley and Miss Williams, who have shown that most of the trouble with syphilitic sera, associated with the use of inadequately standardised and excessively strong extracts, arises in tests on old Wasserman sera. Sarcomatous sera on the other hand have never reacted. Numerous preparations of wet and dry scolices extracted with 70%, 80%, 90% and absolute alcohol have been investigated, and the optimum time for extraction has also been considered. It has been found that owing to the ease with which this specific helminthic substance can be extracted, a short period of treatment with alcohol suffices, and that in two to six hours a highly potent hydatid antigen can be obtained, containing a minimum of Wasserman liquid. A 1% preparation of dried scolices extracted for two to six hours with absolute alcohol, and subsequently standardised in the presence of hydatid, normal and syphilitic sera (fixing not less than 40 M.H.D.'s of complement with Wasserman antigen) has been found reliable from every viewpoint. Observations are being extended over a larger series of cases, and it is expected that this extract will prove a reliable, stable and high titre antigen suitable for universal use.

In contradistinction to its efficacy as a complement fixating antigen, the Director (1924) showed that these alcoholic scolex extracts were poor anaphylactic antigens, and in July last year Dr. Fairley and Miss Williams, finding that the antigenic factor in hydatid fluid was thermostable, employed boiled saline extracts of scolices as an antigen in the intradermal skin test,* with positive results in a number of hydatid cases. An investigation on control cases, however, showed that the scolex extracts sometimes gave rise to pseudo-positive reactions, due no doubt to the presence of pharmacologically active substances. For this reason we prefer to use filtered hydatid fluid for the Casoni test when this is available.

The capacity of both hydatid fluid and scolex extracts to produce antibody *in vivo* has also been studied in experimentally inoculated sheep and goats. Both hydatid fluid and boiled saline scolex extracts are most potent in this regard, and after a series of subcutaneous or intravenous injections, high titre sera are almost invariably obtained (*i.e.*, fixing 30-50 M.H.D.'s in the presence of specific antigen.) Antibody may also be produced by injecting the alcoholic extracts of scolices, but it is never as pronounced as with the saline ones. Furthermore, these studies have shown that boiled saline extracts of *T. saginata* injected into animals produce antibody which reacts in complement fixation tests as readily with hydatid fluid, saline or alcoholic scolex extracts as it does with saginata extract itself, thus proving the essential group nature of the reaction for taenia antigens.

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* We have just received from Professor Fulleborn, of Hamburg, a small sample of dried scolices which he has recently advocated for use in skin tests.

The serum of some of these experimentally inoculated sheep has been separated by Mr. Holden into globulin and albumin fractions, and serological tests show that complement fixation antibody, whether occurring in hydatid or *T. saginata* immunised animals, invariably resides in the globulin fraction.

An interesting, though somewhat disappointing feature, of these experiments has been the difficulty in demonstrating either the intradermal skin reaction of inoculated animals or the formation of specific precipitin in the peripheral blood.

A considerable amount of new work on the intradermal skin test has also been done by Dr. N. Hamilton Fairley and Miss Williams. The use of boiled saline scolex extract as a Casoni antigen has been mentioned, and another feature has been the demonstration of pseudo-positive reactions with sheep hydatid fluid in patients who were sensitive to sheep serum, though not suffering from echinococcosis. The Director has shown the constant presence of sheep serum in hydatid fluid derived from this source, and for these reasons a control injection of sheep serum (1/1,000) is advocated. The stroke test, as described by Lewis, should also be performed, and we regard any patient who reacts by whealing to moderate stroking as unsuitable for the Casoni test.

A detailed analysis of the results of the Casoni and complement fixation reactions performed in Melbourne from 1922-27 has been carried out by Dr. K. D. Fairley, who last year received a grant from the Melbourne University Clinical Research Fund, and several important lines of investigation which were the outcome of this work are now being followed up. These include the acquiring of local sensitisation following several Casoni tests applied to the same skin area in patients free from hydatid disease, the response observed in syphilitics, and the presence of an immediate wheal or delayed response in patients passively sensitised by local intradermal or intravenous injection of serum containing hydatid antibody.

A series of studies on the anaphylacic antigens in hydatid fluid have been carried out by the Director side by side with other researches on complement fixation and on the Casoni test described elsewhere. The first of these papers is concerned with the presence of an anaphylactic antigen other than host serum protein, which, in confirmation of Graetz and others, was shown to be present in most samples of hydatid fluid. This, however, is not necessarily a constituent of the fluid in the living parasite, for (a) it is virtually impossible to remove fluid from within a mother cyst without some of it coming in contact with the adventitia, and (b) in "in vitro" experiments mother and daughter cysts though permeable to dyes of low molecular weight, are not readily permeable to oxyhaemoglobin or to serum proteins. The presence of a second antigenic substance, which is relatively heat stable and presumably of parasitic origin, was demonstrated by using concentrated hydatid fluid from several species of animals, and also by eliminating the bulk of the host protein by heating. This antigen was not filterable through the pyroxylin filters used in these experiments.

The second paper in conjunction with Dr. N. Hamilton Fairley and Miss Williams is concerned with the filterability of the hydatid antigen. The more impermeable filters did not let through either anaphylactic antigen or the substances responsible for complement fixation with antibody-containing sera, or for the Casoni reaction in patients infested wth hydatid. Incidentally Mr. Holden was able to show that these inactive filtrates contained no protein detectable by chemical tests. When more permeable filters which prevented the passage of host serum protein were used for hydatid fluid, the parasitic anaphylactic antigen was filterable, and appeared to take through the filter with it traces of host serum protein. The filtrates only reacted feebly in complement fixation experiments with sera containing antibody, though they gave positive Casoni reactions in patients infested with hydatid. Mr. Holden was able to demonstrate the presence of traces of protein in the filtrates from hydatid fluid but not from host serum. The parallelism in the results of the chemical and anaphylactic tests and of the Casoni reactions suggests that a substance, protein in nature, and capable of reacting as an anaphylactic antigen, may be responsible for the intradermal skin reaction, though the evidence is not conclusive on this point.

It is uncertain whether the substance which reacts in specific hydatid complement fixation reactions is the same or another substance.

KELLAWAY, C. H.:

> "Hydatid Fluid as an Anaphylactic Antigen."
> Journal of Pathology and Bacteriology (1928), **31**, p. 141.

KELLAWAY, C. H.,
FAIRLEY, N. H. and
WILLIAMS, F. E.:

> "The Filterability of Hydatid Antigen."
> (In the Press.)

Some observations by the Director on the use of extracts of liver fluke as anaphylactic antigens will shortly be published. In these experiments, which were directed towards ascertaining the nature of the active antigenic substances in the parasite, a comparison has been made between saline extracts and extracts in alcohol of varying strength. Saline extracts contain pharmacologically active substances which were removed by pressure dialysis, and after this treatment were shown to be excellent antigens both for the production and testing of sensitiveness. Extracts of dry powdered flukes in absolute alcohol, while unsatisfactory for testing the reaction of plain muscle, did occasionally produce in injected animals sensitiveness of slight degree.

Observations on hydatid scolex extracts have also been made with somewhat similar results.

Bilharzia.

Dr. N. Hamilton Fairley and Miss Williams have made a valuable contribution to the diagnosis of bilharzia. They have described an intradermal skin reaction similiar to the Casoni test in hydatid infection. The antigen used is a filtered saline extract of dried powdered liver of snails infested with the cercariae of *S. Spindalis*. For the material the Institute is indebted to Lt.-Colonel F. P. Mackie, O.B.E., I.M.S., who sent it from the Haffkine Institute, Bombay.

The reaction is characterised by the rapid appearance of a large white wheal 2 or 3 cm. in diameter, with pseudopodia-like outrunners and a surrounding zone of erythema. Delayed reactions are manifested by erythema, hotness of the skin, and puffy swelling of the deeper tissues occurring three to twenty-four hours after the initial injection. Seven out of eight patients who were or had been suffering from bilharzia (*Schistosoma haematobium*) contracted in Africa, gave immediate reactions. Three of them also showed responses of delayed type. Out of 47 control patients, 44 failed to give reactions while three gave immediate but not delayed reactions. Each of these three positive control patients gave a triple response to the stroke test, and in consequence any patient showing whealing on firm stroking is regarded as unsuitable for purposes of the intradermal test.

The test is exclusively of diagnostic value, and does not afford any index to the effects of drug treatment. Reactions were given by two patients treated for bilharziasis who were regarded as cured both on serological and clinical grounds. The value of the complement fixation reaction in estimating the endpoint of cure is discussed. The persistence of strong positive reactions several years after treatment is recorded, and in each instance the serological findings are regarded as definitely indicating the persistence of living schistosomes in the host.

FAIRLEY, N. HAMILTON and
WILLIAMS, F. E.:

"A Preliminary Report on an Intradermal Reaction in Schistosoma."

Medical Journal of Australia, December 10th, 1927.

Observations on the complement fixation reaction in bilharzia and on the intradermal skin test are being continued by Dr. Fairley and Miss Williams. Lt.-Colonel F. P. Mackie, O.B.E., I.M.S., and other members of the staff of the Haffkine Institute, Bombay, have generously supplied us with additional material for the preparation of Schistosoma antigens. This includes freshly filtered extracts of bilharzia cercariae, and dessicated adult schistosomes for use in the intradermal skin test, and also alcoholic cercarial extracts for complement fixation reaction. With the co-operation of the Commonwealth Departments of Repatriation and Public Health, a serological survey of cases of bilharzia contracted during the war and located in the different States is about to be undertaken, and it is hoped to present the results of the investigations at the International Congress of Tropical Medicine and Public Health to be held in Cairo in December of this year.

Cancer.

Dr. Thomas Cherry, the Grice Research Fellow, will shortly be publishing the results of his experiments carried out here during the last three years on the occurrence of cancer and allied neoplasms in mice which have been inoculated intradermally with minute doses of tubercle bacilli. Ninety-six mice so inoculated have died at an average time of 8½ months after this treatment (average age at death, 15½ months). Forty-one of these were found to have epithelial tumours, eighteen sarcomata or lymphosarcomata, and five lyphomata. A notable feature in sixty of the animals was the enlargement of the lymph glands of the neck, axilla, mediastinum and gastro-splenic region. There was frequently enlargement of the spleen and lymphocytic infiltration of the bone marrow, pancreas, stomach and liver.

One hundred and twenty-eight control mice died at an average age of 16½ months. There were four with epithelial tumours, four with lymphosarcomata, and fourteen with lymphomata. In twenty-three the lymph glands were enlarged.

These results, if substantiated by further work, are highly significant, and Dr. Cherry has put forward the view that chronic lymphocytic reactions produced by the tubercle bacillus in these animals have provided a specific stimulus to malignant growth, more especially of epithelial type.

Dr. Cherry has also described granulomata, in which acid fast bacilli were found, arising at the site of inoculation in three of his experimental mice. In 10 other animals acid fast bacilli were found in the spleen, lymph glands or other organs. These observations are also of great interest, as hitherto the mouse has been regarded as resistant to the tubercle bacillus, even when very large numbers of organisms have been injected. The extensive changes in the lymphatic system in so many of the experimental animals are clearly related to the injection. Dr. Cherry's control mice are divided into two groups; in the smaller, of fifty-six animals, the milk administered as part of their diet was unboiled. Of these animals sixteen had enlarged lymph glands; ten, lymphomata; four, sarcomata or lymphosarcomata; and two, epithelial tumours. In the larger group of eighty-two, the milk in whose diet was boiled, there were only seven with enlarged glands, four with lymphomata, and two with epithelial tumours. While these differences may possibly be associated with the presence of tubercle bacilli in some samples of unboiled milk, it is probable that improvement in the conditions of life in the later series of eighty-two mice may have played some part in producing this result.

Mr. Henry Searby, who is in receipt of a grant from the Commonwealth Government, is continuing his analysis of the cases of cancer treated at the Melbourne Hospital since 1921. This work, which is not yet completed, will, it is hoped, afford useful information in regard to the regional distribution of cancer among the hospital population, the expectation of life in treated and untreated cases, and the effect of delay in coming for treatment.

Initial experiments made by Dr. Fairley and Miss Williams to determine the applicability of the modern complement fixation reaction to the serological diagnosis of cancer have not been promising. Saline and alcoholic extracts of carcinomata have been utilised as antigens, but the results in a series of cases of cancer have been uniformly negative. Moreover, as is commonly the case with tissue extracts, positive results were obtained with syphilitic sera when the antigens were used in low dilutions. Observations are being continued, and the value of other organic solvents in the preparation of the different extracts is being explored. For this work the collection of sterile tumours and of sera is being carried out by Dr. Cooper.

Morbid Anatomy.

Dr. Wright Smith, during the course of the year, has performed the great majority of the routine autopsies. During this period 542 post mortem examinations were held, and of these 444 were done by him. Six hundred and sixty-two routine histological examinations for diagnosis of pathological conditions have been made. Dr. C. H. Mollison, assisted by Dr. Wright Smith, has been responsible for this part of our activities. In addition, studies of two rare pathological conditions by Dr. Wright Smith with Dr. G. R. Cameron were published this year, and Dr. Wright Smith has put on record a case of gummata of the aorta which resulted in death from rupture into the pericardium.

CAMERON, G. R., and
WRIGHT SMITH, R. J.:

"Diffuse Gastric Polyposis Accompanying Carcinoma of the Pancreas."
Medical Journal of Australia, August 20th, 1927.

WRIGHT SMITH, R. J.:

"Carcinoma of the Stomach with Associated Cerebral Melano-endothelioma and Early Medullary Carcinoma of a Bronchus."

Medical Journal of Australia, August 20th, 1927.

WRIGHT SMITH, R. J.:

"Gummata of the Aorta with Rupture into the Pericardium."

Journal of Pathology and Bacteriology. (In the Press.)

Sarcomatous Tumour of the Testicle.

Mr. H. R. Dew, who in 1923 won the Jacksonian Prize of the Royal College of Surgeons, England, with his essay on "Malignant Tumours of the Testicle," has this year contributed a careful histological study of a further series of five of the rare sarcomatous tumours of this region. These illustrate the various possible origins of these tumours; within a teratomata, from the intertubular connective tissue of the testis, from the covering tissues, and, finally, as secondary metatases following growths elsewhere.

DEW, H. R.:

"Sarcomatous Tumours of the Testicle."
Surgery, Gynaecology and Obstetrics. April, 1928.
Pages 447-458.

The Pathology of Pyorrhoea Gingivae.

Dr. J. Monahan Lewis, using material partly obtained by Professor F. C. Wilkinson and partly from his own private practice, has during the last two years been engaged on a histological study of the changes met with in this disease. This work is now completed.

Incidentally, he has described a specialised, structureless "intermediary substance" strictly confined to the area of the tooth uncovered by enamel, and lying between the cementum and the gum epithelium. He regards this as the cause of the firm adhesion which normally exists between the epithelium and the cementum, and as probably being derived by cornification of the epithelium. It is independent of, and not continuous with, the "tooth cuticle" described by Gottlieb.

The histology of pyorrhoea gingivae has been carefully described by Lewis, and in the main his description is in accord with the work of Gottlieb, Hopewell-Smith and others. He prefers this name to the more common "pyorrhoea alveolaris," as indicating the seat of the predominant pathological changes. He stresses the early naked-eye appearances presented by the gums, the loss of "matt" surface, and the replacement of their normal pallor by a purple colour of varying depth exhibiting downgrowths and sometimes a network of columns of epithelium, the spaces being filled with connective tissue. Subgingival calculus does not, according to Lewis, play any large part in the process, and may exist in close contact with undamaged gingival epithelium which is moulded to its surface. The "break" in the epithelium of the "trough" does not occur at the bottom but nearer the free edge of the gum margin.

There is congestion and oedema of the connective tissue, with well-defined areas of small cell reaction and many plasma cells. The changes in the peridental membrane are by contrast slight. There is an increase in its vascularity, and in advanced conditions destruction of some of the principal fibres, which are replaced by irregularly arranged fibrous tissue.

The changes in the bony alveolar margins are mainly those of rarefaction, the inorganic salts being leached out of the matrix. The only regeneration which occurs in this tissue appears to be dependent on replacement of the salts.

LEWIS, J. M.:

"Some Observations on the Pathology of Pyorrhoea Gingivae."

Australian Journal of Dentistry. Volume 31. December, 1927.

Tubercular Disease of the Hip Joint.

Dr. C. J. O. Brown has completed a careful study of the end results in sixty cases of undoubted tuberculosis of the hip joint. In sixteen of these, good functional results were obtained, fourteen of which have recovered with immobile hip joints, due to bony or fibrous ankylosis. Nine cases are unsatisfactory from various causes — interference with growth or gross bony destruction with loss of articular surfaces, attended by deformity and subluxation of the joint. Thirteen deaths have been traced, six from tubercular meningitis and one from amyloid. Twenty-one cases are still undergoing treatment. Seven are doing well, and will probably eventually become quiescent. In six the disease is still very active, and two of these have many sinuses and are in an advanced stage of amyloid disease. Seven cases with an average time of onset of twenty-one years have been quiescent, and have relapsed one or more times, and furnish examples of apparent cure with loose fibrous ankylosis. The remaining case was healed for two years and was discharged two and a half years, but now has tuberculosis of the other hip.

Apart from these, there were twelve cases without radiological evidence of bone destruction, which may or may not have been tubercular in origin. Complete recovery is likely to occur in this type of case.

Dr. Brown concludes that bony ankylosis is the best result which can be achieved in frank tuberculosis of the hip joint, and that the best position is 30° to 35° flexion without abduction, adduction or rotation. When the end result is a fibrous ankylosis with a fair range of movement this is unsatisfactory, since such mobile hips are weak, inefficient and liable to relapse even many years after apparent cure. Treatment should be by traction and abduction until all activity has subsided. If, then, the articular surfaces be intact, mobility should be encouraged, otherwise prolonged fixation in plaster should be used to obtain bony ankylosis.

BROWN, C. J. O.:

> "The Diagnosis and End Results of Tuberculosis of the Hip Joint."
>
> Medical Journal of Australia. (In the Press.)

Basal Metabolism.

Dr. J. F. Chambers is at present engaged in the analysis of 575 patients in whom he has made over 1,000 basal metabolic determinations during the last 5½ years at this Institute. They include 214 cases of frank hyperthyroidism, 221 of doubtful hyperthyroidism, 23 cases of myxoedema, 75 with some degree of hypothyroidism or of hypopituitarism, 21 cases of non-thyrotoxic goitre and a small miscellaneous group of 21 cases.

In addition, he has studied 50 normal individuals with special reference to the question of the applicability of American standards to Victorian conditions, the range of variation exhibited by healthy individuals, and the influence exerted by "physiological training" of the individuals tested. Finally, he is able to compare his observations on normal subjects here with similar observations by him in England. The results of this work on normal subjects were embodied in a report to the Conference on International Metabolism held in Sydney under the auspices of the Australian National Research Council during the recent visit of Professor Earle.

Routine Work.

A new departure is being made in the coming year by the appointment of Dr. Lucy Bryce to take charge of the routine bacteriological work of the hospital, which has hitherto been largely carried out by successive Pathological Registrars. Arrangements are also being made to do allergic skin tests here. Previously this work has been done in the Out-Patient Department by Dr. Ivan Maxwell.

The routine bio-chemical work is continually increasing, but Miss Splatt has for the last few months had the advantage of the voluntary assistance of Miss M. Shannon. Basal metabolic rate determinations and electro-cardiography have been done by Miss Cecil Maudsley, who, in addition, has been responsible for most of the photographic work of the Institute.

The routine serological work has been carried out, as heretofore, by Miss F. E. Williams, and has included complement fixation tests for hydatid disease and for gonococcal and syphilitic infections.

The Museum.

The Museum, which now contains 500 colour preparations fully described and catalogued, with a corresponding collection of excellent microscopic preparations, is under the care of Dr. Wright Smith. Various improvements in arrangement have been made. The specimens have been displayed better by the use of dull black backgrounds in the cases, and are now viewed by artificial light.

Interesting specimens which have been added during the past year include an osteitis fibrosa of the skull, a series of melanomata, two cases of Hodgkin's sarcoma, lymphosarcomata of testes, ruptured gumma of aorta, mycotic aneurism of the splenic artery, tuberculous pericarditis, adrenal carcinoma in an infant, a chromophobe adenoma of the pituitary gland, pancreatic calculi with atrophy of the pancreas, several cases of hydatid of the liver, diffuse gastric polyposis, sarcoma of the stomach and adenoma in a Meckel's Diverticulum.

In addition, a series of twenty-five Australian and five Indian snakes and thirteen preparations illustrating hydatid disease in the sheep, pig and ox have been mounted in colour. We are particularly indebted to Dr. C. H. Mollison, Dr. R. W. Chambers, Mr. H. R. Dew and Dr. F. Gill for valuable specimens.

The Museum has been much used this year by University teachers and clinical lecturers. A special series of tutorials in pathology for the M.S. degree, arranged by the Melbourne Permanent Committee for Post-Graduate Work and conducted by Dr. C. J. O. Brown, has been held here.

The Library.

The Institute Library, which was founded in 1924 by the Edward Wilson ("The Argus") Trust, is becoming increasingly useful as the gaps in our series of journals are being filled. In this work it is a pleasure to acknowledge our indebtedness to Miss K. Baverstock, the Librarian of the National Institute of Medical Research, London, who, as in previous years, has helped us greatly in procuring missing numbers and volumes. Our thanks are also due to the following for gifts of periodicals or books: L'Académie royale de Médecine de Belgique, the Commonwealth Department of Public Health, the Council of Scientific and Industrial Research, the Melbourne University Medical Library, the National Institute of Medical Research (London), la Societé royale des Sciences médicales et naturelles de Bruxelles, the Rockefeller Institute (New York).

FINANCIAL STATEMENT FOR YEAR ENDED 30th JUNE, 1928.

Receipts.

Balance brought forward from 30th June, 1927		£3,392 6 6
Trustees, Hall Trust	£3,150 0 0	
University of Melbourne—		
Refund, Exp. Cancer Research Fellow	72 18 0	
Refund, Exp., Obstetric Research	150 0 0	
Donation, Felton Bequest Committee	300 0 0	
Other Donations	100 3 3	
Interest on Investments	149 8 6	
Commonwealth Government—		
Refund *re* Bundaberg Commission	365 10 8	
Special Grant for Cancer Research	150 0 0	
Research Grant	2,500 0 0	
		6,938 0 5
		£10,330 6 11

Expenditure.

Materials Account		£423 12 10	
Apparatus	£279 2 0		
Less Fees, etc.	140 5 10		
		138 16 2	
Salaries and Wages		4,800 11 6	
Repairs to Apparatus		10 11 5	
Fittings and Equipment		229 0 6	
Buildings, Equipment		35 8 0	
Repairs to Buildings		26 2 4	
Sundries		260 5 11	
Advances to Library (making a total of £129/10/9)		76 5 7	
Travelling Expenses, Dr. Burnet		120 9 1	
			£6,121 3 4
Balance, Fixed Deposit, Bank of N.S.W.		£2,600 0 0	
Deposit at Call, T. Wragge's Estate		3,000 0 0	
Current A/c., E. S. & A. Bank		60 0 0	
		£5,660 0 0	
Less Overdrawn, Bk. of N.S.W.		1,450 16 5	
			4,209 3 7
			£10,330 6 11

BIO-CHEMICAL DEPARTMENT—ENDOWMENT ACCOUNT.

Balance brought forward from 30th June, 1927	£7,363 19 6	Commission for Collecting Interest		£1 0 0
Donations	274 3 0	Balance—		
Interest on Investments	481 10 0	£500 C'wlth. Ins. Stock, 5%	£500 0 0	
		£1,500 M.M.B.W. Stock, 4%	1,218 4 3	
		£1,800 M.M.B.W. Stock, 6½%	1,952 11 1	
		£140 Vic. Gov. Ins. Stock, 5¼%	140 0 0	5
		£800 City of Melb. Deb., 5½%	807 12 2	
		£2,550 Mortgage, M. Anthony, 6%	2,550 0 0	
		Current A/c., Bk. of N.S.W.	950 5 0	
				8,118 12 6
	£8,119 12 6			£8,119 12 6

LIBRARY ACCOUNT.

Balance brought forward from 30th June, 1927	£2,000 0 0	Books, Journals, Bookbinding, etc.		£206 5 7
Interest on Investments	130 0 0	Balance—		
Advance from Working A/c. (Total, £129/10/9)	76 5 7	C'wlth. War Bond, 6%	£1,000 0 0	
		Mortgage, Montgomery, 7%	1,000 0 0	
				2,000 0 0
	£2,206 5 7			£2,206 5 7

BIO-CHEMICAL DEPARTMENT ACCOUNT.

Balance brought forward from 30th June, 1927		£677 7 5	Salaries, Wages	£818 15 6	
Donations,			Materials	148 18 10	
Edward Wilson Trustees	£1,500 0 0		Apparatus	9 11 8	
Interest on Investments	10 0 0		Sundries	59 15 6	
		1,510 0 0			£1,037 1 6
			Balance—		
			Cash with Agent-General, London	£129 8 2	
			Current A/c., Bk. of N.S.W.	1,020 17 9	
					1,150 5 11
		£2,187 7 5			£2,187 7 5

Note.—Against this balance there are liabilities outstanding amounting to £400.

Auditors' Report.

I have to report that I have completed the audit of the books and accounts of the Institute for the period ended 30th June, 1928. I have verified all receipts and have had vouchers produced for all disbursements. All information and explanations required have been given. The statement is a correct statement of receipts and expenditure as revealed by the books of the Institute.

Dated, July 11th, 1928.

W. M. JARVIE, F.F.I.A., Auditor.